UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/578,162	11/29/2006	Tonia Sue Agin	PC25353A	4630

25533 7590 11/03/2009

PHARMACIA & UPJOHN
7000 Portage Road
KZO-300-104
KALAMAZOO, MI 49001

EXAMINER	
GRASER, JENNIFER E	
ART UNIT	**PAPER NUMBER**
1645	

NOTIFICATION DATE	DELIVERY MODE
11/03/2009	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

~IPGSKala@Pfizer.com

Office Action Summary	Application No.	Applicant(s)	
	10/578,162	AGIN ET AL.	
	Examiner	Art Unit	
	Jennifer E. Graser	1645	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *7/20/09*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-20* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-20* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *7/20/09*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office Action.

Acknowledgment and entry of the Repsonse submitted on 7/20/09 is made. Claims 1-20 are currently pending.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

1. Claims 1-4, 13-17, 19 and 20 are rejected under 35 U.S.C. 102(b) as being anticipated by Thoma et al (US 6,440,408 B2).

Thoma et al teach a method of producing active immunity (which includes inducing an immune response) against a bacterial or protozoal disease in a subject which comprises administering a live bacteria along with an antibody. Column 3, lines 49-50 teach that by 'live' is meant not killed. Column 4, second full paragraph, teaches immunization of birds, including chickens, turkey and a duck. Column 4, line 43, teaches that the bacteria may be Campylobacter jejuni. Column 5, fourth full paragraph teaches *in ovo* immunization of the vaccine which should occur preferably in the fourth quarter of incubation which for chicken eggs is on about the 15th-19th day of incubation and turkey eggs on or about the 21st-26th day of incubation. The use of

pharmaceutically acceptable carriers is taught at the bottom of column 6. The top of column 7 teaches the use of one of more adjuvants.

Response to Applicants' arguments:

Applicants argue that Thoma teaches the use of a neutralizing antibody with their live bacterial vaccine. They argue that the prior art has taught that live bacterial vaccines are unsafe and should not be administered to eggs which is why Thoma includes a neutralizing antibody in their vaccines. This argument has been fully and carefully considered but is not deemed persuasive. The instant claims allow for the inclusion of additional ingredients given the open language, e.g., the neutralizing antibody. Additionally, the methods instantly claimed merely teach the use of live cells of any Campylobacter species which was used in the prior art (whether or not this had some negative results to some of the eggs immunized and some positive results). There does not appear to be anything structurally different to the composition of the instant claims to allow for it to be safely administered. Live cell vaccines to bacteria have been known in the prior art for quite sometime.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

2. Claims 1-4, 6-8, and 13-15 are rejected under 35 U.S.C. 103(a) as being unpatentable over Noor et al (British Poultry Science, 1995. 36(4): 563-573) in view of

Ziprin et al (Poultry Science, vol. 78, No. SUPPL 1, 1999, page 39, 88th Annual Meeting of the Poultry Science Association, Inc., Springsdale, Arkansas, USA,; August 8-11, 1999).

Noor et al disclose *in ovo* oral vaccination of chicken eggs with Campylobacter, specifically C.jejuni, which is heat inactivated, at day 16 of incubation (i.e., final quarter of incubation). See abstract. Noor et al teach that the advantages of in ovo immunization in establishing early immunity are note associated with adverse effects on hatchability or postnatal weight gain. Noor et al teach that in ovo vaccination has been previously reported to induce a higher antibody response in chicks than in postnatal exposure and also resulted in significant improvement in performance. See p. 564, 2nd full paragraph. However, Noor et al do not particularly exemplify the use of live Campylobacter strains in their methods.

Ziprin e al disclose the *in ovo* administration of various live strains of C.jejuni and the effects of mutations in C.jejuni genes on cecal colonization and liver invasion when given in ovo or on day of hatch. Ziprin teach that none of the strains caused morbidity on i.p. challenge though the doses were high. Ziprin teach that by determining the role of the genes studied in colonization, they hope to find some means to prevent C.jejuni from establishing in the gastrointestinal tract of chickens. Several different genetically modified strains were used. Ziprin specifically teach strains with heterologous polynucleotide seqeunces that encode proteins essential in colonization of domesticated birds by Campylobacter, e.g, *dnaJ* and *cadF* (as outlined on page 3, lines 19-20 of the instant specification). See abstract.

Noor et al teaches the in ovo vaccination of poultry against Campylobacter and Ziprin teaches that the delivery of live, attenuated campylobacter strains in ovo was known in the prior art. It would have been prima facie obvious to one of ordinary skill in

the art to substitute a live, especially a live attenuated strain, for the heat-inactivated strain used in the Noor et al reference because Ziprin teaches that live cells of Campylobacter may be administered in ovo and one of ordinary skill in the art would expect a live, attenuated strain of Campylobacter to provide similar immunogenic results as the heat inactivated strain of Campylobacter. Further, a live attenuated strain would have the ability to be manipulated to produce additional antigens to increase the spectrum of the immune response. A "physiologically acceptable carrier" reads on water and therefore would be inherent in the preparation of the cells for immunization.

Response to Applicants' arguments of all of the outstanding 103 rejections (also the 2 below):

Applicants argue that avian species are not expected to mount vigorous immune responses against a microorganism that generally causes them no harm. They argue, as also outlined by the Examiner, that Noor does not teach live vaccines and they further argue that Ziprin et al only disclose colonization experiments with live strains with the intent of finding methods to prevent colonization which is not the same thing as inducing an immune response. They argue that Ziprin discloses that in ovo challenge using live cells can lead to persistently infected birds.

In response to applicant's arguments against the references individually, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.,* 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986). Additionally, the methods instantly claimed merely teach the use of live cells of

any Campylobacter species which was used in the prior art, whether this had some negative results to some of the eggs immunized and some positive results. There does not appear to be anything structurally different to the composition of the instant claims to allow for it to be safely administered. Accordingly, the method and materials in the instant claims are identical to the that in ovo challenge using live cells which lead to persistently infected birds of Ziprin. Live cell vaccines to bacteria have been known in the prior art for quite sometime.

Ziprin e al disclose the *in ovo* administration of various live strains of C.jejuni and the effects of mutations in C.jejuni genes on cecal colonization and liver invasion when given in ovo or on day of hatch. Ziprin teach that none of the strains caused morbidity on i.p. challenge though the doses were high. . It would have been prima facie obvious to one of ordinary skill in the art to substitute a live, especially a live attenuated strain, for the heat-inactivated strain used in the Noor et al reference because Ziprin teaches that live cells of Campylobacter may be administered in ovo and one of ordinary skill in the art would expect a live, attenuated strain of Campylobacter to provide similar immunogenic results as the heat inactivated strain of Campylobacter. Further, a live attenuated strain would have the ability to be manipulated to produce additional antigens to increase the spectrum of the immune response. Applicants argue that live cell vaccine is not safe, yet they provide the same live cells that were taught in the prior art, e.g,. the vaccine used in the claimed methods is not attenuated or altered in any manner.

Applicants have cited the Mead et al reference, not cited by the Examiner, for its teachings that Campylobacter rarely cause disease in poultry and that avian species are not expected to mount vigorous immune responses against a microorganism that generally causes them no harm. The Mead et al reference has been reviewed in context. Its teachings that 'there is production of specific immunoglobulin' upon infection demonstrates that the live cells can effectively 'induce an immune response in birds' as instantly claimed. There is no requirement of effecting levels of intestinal carriage or susceptibility to infection as argued by Applicants. Those arguments are not commensurate in scope with the claimed invention.

3. Claims 5, 16, 17, 19 and 20 are rejected under 35 U.S.C. 103(a) as being unpatentable over Noor et al (British Poultry Science, 1995. 36(4): 563-573) in view of Ziprin et al (Poultry Science, vol. 78, No. SUPPL 1, 1999, page 39, 88th Annual Meeting of the Poultry Science Association, Inc., Springsdale, Arkansas, USA,; August 8-11, 1999), as applied to claims 1-4, 6-8 and 13-15 above and further in view of Ziprin et al (Current Microbiol. 2002. 44: 221-223)..

The teachings of Noor et al and Ziprin et al (Brit. PS) are set forth above. However, they do not specifically teach the additional use of an adjuvant of the use of more than one species in their compositions.

Ziprin et al teach that the prior art has suggested that avirulent viable cell vaccines should be tried for protection against C.jejuni. See first paragraph on page 221. The reference teaches combining several non-colonizing strains of Campylobacter in a 'vaccine cocktail" so that chicks can be exposed to all surface proteins on wild-type

colonizing strains. See second paragraph, column 1 on page 221. Ziprin et al teach the use of viable-cell bacterial suspensions and the use of Ribis's adjuvant. See second column on page 221. The references teaches that 'much previous work has demonstrated that antibody production occurs when embryonated eggs are vaccinated, e.g., *in ovo* vaccination, and cell mediated immune responses 'turn on' about three days after hatch. The instant reference teaches the vaccination of hatched chicks and did not achieve the same results as previous work using *in ovo* administration.

It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made that more than one strain/species of Campylobacter could be used in the method taught by the combination of Noor et al and Ziprin et al (Brit. PS) because Noor et al teach success with the use of a single strain and Ziprin et al (Curr.Microbiol) teaches that combining several non-colonizing strains of Campylobacter in a 'vaccine cocktail" would allow for exposure to all surface proteins on wild-type colonizing strains which would thereby provide for a wider spectrum of coverage against disease factors. Absent evidence to the contrary, the use of multiple species would be expected to raise a more varied immune response. Additionally, the use of an adjuvant in a vaccine composition would have been an obvious addition to enhance the immune response to the vaccine taught by Noor et al and Ziprin et al (Curr.Microbiol) specifically teach the use of Ribis's adjuvant in its Campylobacter vaccines.

4. Claims 9-12 and 18 are rejected under 35 U.S.C. 103(a) as being unpatentable over Noor et al (British Poultry Science, 1995. 36(4): 563-573) in view of Ziprin et al

(Poultry Science, vol. 78, No. SUPPL 1, 1999, page 39, 88th Annual Meeting of the Poultry Science Association, Inc., Springsdale, Arkansas, USA,; August 8-11, 1999), as applied to claims 1-4, 6-8 and 13-15 above, in further view of Yokogawa et al (Us 6,410,222 B1).

The teachings of Noor et al and Ziprin et al (Brit. PS) are set forth above. However, they do not specifically teach the additional use of a heterologous antigen from a virus, bacteria or parasite that causes disease in a domesticated bird, or an antigen from an organism that causes food-borne illness in humans, or a protein that can enhance growth or feed efficiency of a domesticated bird.

Yokogawa et al teach the in ovo vaccination of marek's disease type 1 virus. Marek's disease is a chicken infectious disease. Yokogawa et al teach the use of attenuated live viruses into egss in the fourth quarter of incubation. The use of a mixed vaccine is specifically taught from other viruses or bacteria, including Campylobacter spp.. See column 4, lines 36-49. The use of additional antigens are also taught throughout column 4 and the top of column 5 and in the claims.

It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made that the additional use of a heterologous antigen from a virus, bacteria or parasite that causes disease in a domesticated bird, or an antigen from an organism that causes food-borne illness in humans, or a protein that can enhance growth or feed efficiency of a domesticated bird could be added to the vaccines taught by Noor et al and Ziprin et al (Brit. PS) because multivalent vaccines were well known in the art at the time the invention was made as a means to allow for a

broader spectrum of protection against disease with fewer inoculations. Yokogawa et al is cited to show that, absent evidence to the contrary, the use of an additional antigen would have been an obvious design choice serving to broaden the spectrum of the immune response. Yokogawa et al specifically teaches the use of a mixed vaccine in their live attenuated Marek virus vaccine (for in ovo vaccination) which includes other viruses or bacteria, including Campylobacter spp.. The use of additional antigens against food-borne illness or diseases found in birds would have been obvious choices as heterologous antigens in the vaccines taught by Noor and Ziprin because chickens are consumed by humans and one would want to prevent these types of infections for the safety of the food supply.

1. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Correspondence regarding this application should be directed to Group Art Unit 1645. Papers related to this application may be submitted to Group 1600 by facsimile transmission. Papers should be faxed to Group 1600 via the PTO Fax Center located in Remsen. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November

15,1989). The Group 1645 Fax number is 571-273-8300 which is able to receive transmissions 24 hours/day, 7 days/week.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jennifer E. Graser whose telephone number is (571) 272-0858. The examiner can normally be reached on Monday-Thursday from 8:00 AM-6:30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Robert Mondesi, can be reached on (571) 272-0956.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (571) 272-0500.

/Jennifer E. Graser/
Primary Examiner, Art Unit 1645

10/28/09